UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte HENRY YUE, PREETI LAL, Y. TOM TANG, DYUNG AINA M. LU, and JANICE AU-YOUNG

Appeal No. 2004-1385
Application No. 09/525,867

ON BRIEF

Before WINTERS, ADAMS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claim 31. Claims 3-6, 8, 10-14, 23, 26-30, and 32-36 are also pending and have either been allowed (claims 3-6 and 8) or withdrawn (claims 10-14, 23, 26-30, and 32-36). Claim 31 reads as follows:

31. An isolated polynucleotide selected from the group consisting of:

a) a polynucleotide comprising the polynucleotide sequence of SEQ ID NO:9,

b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 80% identical to the polynucleotide sequence of SEQ ID NO:9 over the entire length of SEQ ID NO:9,

c) a polynucleotide completely complementary to a polynucleotide of a),

d) a polynucleotide completely complementary to a polynucleotide of b), and

e) an RNA equivalent of a)-d).

The examiner relies on the following references:

Van de Loo et al., "An oleate 12-hydroxylase from Ricinus communis L. is a fatty acyl desaturase homolog," Proc. Natl. Acad. Sci. USA, Vol. 92, pp. 6743-6747 (1995)

Brenner et al., "Errors in genome annotation," TIG, Vol. 15, No. 4, pp. 132-133 (1999)

Witkowski et al., "Conversion of a β-Ketoacyl Synthase to a Malonyl Decarboxylase by Replacement of the Active-Site Cysteine with Glutamine," Biochemistry, Vol. 38, pp. 11643-11650 (1999)

Bork, "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle," Genome Research, Vol. 10, pp. 398-400 (2000)

Broun et al., "Catalytic plasticity of fatty acid modification enzymes underlying chemical diversity of plant lipids," Science, Vol. 282, pp. 1315-1317 (1998)

Seffernick et al., "Melamine Deaminase and Atrazine Chlorohydrolase: 98 Percent Identical but Functionally Different," Journal of Bacteriology, Vol. 183, No. 8, pp. 2405-2410 (2001)

Claim 31 stands rejected under 35 U.S.C. § 112, first paragraph, as nonenabled and lacking an adequate written description in the specification.

We vacate the examiner's rejections and enter a new rejection under the second paragraph of 35 U.S.C. § 112.

Background

"Mitochondria are the primary sites of energy production in cells." Specification, page 1. "Mitochondrial dysfunction leads to impaired calcium buffering, generation of free radicals that may participate in deleterious intracellular and extracellular processes, changes in mitochondrial permeability, and oxidative damage which is observed in several neurodegenerative diseases." Page 2. The specification also discloses that "mitochondrial dysfunction often leads to heart disease" and that "[m]itochondria are implicated in disorders of cell proliferation." Id.

The specification discloses eight mitochondrial polypeptides, which have the amino acid sequences shown in the specification's SEQ ID NO:1 through SEQ ID NO:8. The protein of SEQ ID NO:1, which is encoded by the DNA sequence of SEQ ID NO:9, has 213 amino acids and is disclosed to be the "PSST subunit of the NADH:ubiquinone oxidoreductase complex." Table 2.

Discussion

Claim 31 is written in Markush format and is directed to a polynucleotide that "comprises the polynucleotide sequence of SEQ ID NO:9" or "a naturally occurring polynucleotide sequence at least 80% identical to the polynucleotide sequence of SEQ ID NO:9 over the entire length of SEQ ID NO:9," polynucleotides "completely complementary" to the above sequences, or "an RNA equivalent" of the above polynucleotides.

The examiner rejected the claims on the basis that the genus of "naturally occurring . . . 80% identical" sequences (as well as sequences complementary to them and RNA equivalents) was not enabled or supported by an adequate written description.

However, we find these embodiments of the claim to be indefinite and therefore vacate the examiner's rejections and enter a new rejection on that basis. See In re Moore, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971) (Analysis of a claim under § 112 "should begin with the determination of whether the claims satisfy the requirements of the second paragraph. . . . [T]he claims must be analyzed first in order to determine exactly what subject matter they encompass.").

New Ground of Rejection

Under the provisions of 37 CFR § 41.50(b), we enter the following new ground of rejection: claim 31 is rejected under 35 U.S.C. § 112, second paragraph, as indefinite. The scope of the claim is indefinite because of its recitation of "a naturally occurring polynucleotide sequence at least 80% identical to the polynucleotide sequence of SEQ ID NO:9 over the entire length of SEQ ID NO:9, . . . [and] an RNA equivalent [thereof]."

The normal meaning of "polynucleotide" is a polymer made up of nucleotides. Nucleotides are made up of a purine or pyrimidine base joined to a sugar residue (deoxyribose in DNA, ribose in RNA) and a phosphate group. Thus, according to its normal meaning, part (b) of claim 31 would encompass both DNA and RNA. Read in light of the rest of the claim and the specification, however, the scope of the claim becomes unclear.

First, SEQ ID NO:9 is a DNA sequence since it contains thymine (T) residues. The equivalent RNA sequence would have uracil (U) in place of thymidine. The specification defines "percent identity" as follows:

> The phrases "percent identity" and "% identity," as applied to polynucleotide sequences, refer to the percentage of residue matches

> between at least two polynucleotide sequences aligned using a standardized algorithm.

Page 11. The specification provides further discussion of the algorithms CLUSTAL V and BLAST (pages 11-12) but that discussion does not make clear whether the standardized algorithms used in the art to compare sequences recognize T and U as "identical". Thus, it is unclear whether T and U would be considered to be "identical" residues in computing whether a given polynucleotide was "80% identical" to SEQ ID NO:9.

Second, if part (b) of claim 31 is intended to include both DNA and RNA, then part (e) of the claim is entirely superfluous. That is, there would be no need for a part (e) directed to "RNA equivalent[s]" unless parts (a) through (d) of claim 31 are intended to be limited to DNA, rather than encompassing both DNA and RNA. The specification makes clear that the term "RNA equivalent" is used in reference to a DNA sequence. See page 17: "An 'RNA equivalent,' in reference to a DNA sequence, is composed of the same linear sequence of nucleotides as the reference DNA sequence with the exception that all occurrences of the base thymine are replaced with uracil, and the sugar backbone is composed of ribose instead of deoxyribose."

These factors suggest that claim 31 uses the term "polynucleotide" as a synonym for DNA, rather than using it in its usual sense of encompassing both DNA and RNA. However, construing part (b) of the claim as limited to DNA presents its own problems. If part (b) of claim 31 were construed to encompass only "naturally occurring [DNA] sequence[s] at least 80% identical to the [DNA] sequence of SEQ ID NO:9 over the

entire length of SEQ ID NO:9", that part of the claim would very likely define a compound that does not exist.

The DNA shown in the specification's SEQ ID NO:9 is a cDNA sequence. See, for example, page 5, lines 30-32: "Table 1 shows polypeptide and nucleotide sequence identification numbers (SEQ ID NOs), clone identification numbers (clone IDs), cDNA libraries, and cDNA fragments used to assemble full-length sequences encoding MITP" (emphases added). See also working examples I and II (headed "Construction of cDNA Libraries" and "Isolation of cDNA Clones," respectively).

cDNA sequences are not naturally occurring. They are laboratory-made DNA copies of naturally occurring messenger RNA (mRNA) sequences. See, e.g., Darnell, pages 248-254.[1] The only naturally occurring DNA sequence that encodes the protein of SEQ ID NO:1 is a genomic sequence. That genomic sequence is then transcribed by the cell into an RNA equivalent that is processed and eventually translated into the polypeptide of SEQ ID NO:1. The processing steps required to generate an mRNA from a genomic DNA include removal of intervening sequences, or introns.

Virtually all human genes include introns. See Avers, page 243 ("For virtually every eukaryotic gene that has been sequenced, the region between the initiation and termination codons consists of coding regions interrupted by noncoding regions. In these interrupted genes, coding sequences, or exons, are interspersed with noncoding

[1] Darnell et al., Molecular Cell Biology, Scientific American Books, 1986. Copy attached.

intervening sequences, or introns, in the genetic message.").[2] In fact, human genes on average contain about eight introns and nine exons. See Sakharkar (abstract).[3]

Thus, those skilled in the art would expect that the naturally occurring gene encoding the polypeptide of SEQ ID NO:1 would be interrupted by several introns. As a result, those skilled in the art would expect that, more likely than not, no naturally occurring DNA would be 80% identical to SEQ ID NO:9 over the full length of SEQ ID NO:9, because the parts of the naturally occurring gene that are identical to SEQ ID NO:9 would be interrupted by introns that are not part of the cDNA sequence of SEQ ID NO:9.

The naturally occurring gene that encodes the polypeptide of SEQ ID NO:1 would only fall within the scope of part (b) of claim 31 if it has introns that comprise 20% or less of its sequence. If the naturally occurring gene contains greater than 20% introns, it would appear that there is no naturally occurring DNA sequence that is 80% identical to SEQ ID NO:9 over its entire length. Thus, if part (b) of the claim – over which so much time and ink have been spent – is construed as being limited to DNA, it is overwhelmingly likely to be a nullity. It would add nothing to the scope of the claim.

On the other hand, if part (b) of claim 31 were construed to encompass both DNA and RNA, in addition to the ambiguities discussed above (pages 4-5), it would present issues of enablement that have not been discussed on the record to this point. That is, if the claim encompasses both DNA and RNA, and if the corresponding genomic DNA does not contain an anomalously small amount of intron DNA, the only "naturally

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[2] Avers, Genetics, 2nd edition, Willard Grant Press, 1984. Copy attached.

occurring" polynucleotides that would be 80% identical to SEQ ID NO:9 over its entire length would be mRNAs (which are processed to excise introns).

Claim 31 is directed to an "isolated" polynucleotide, but the specification provides no guidance on how to isolate the particular mRNA corresponding to SEQ ID NO:9. Thus, if part (b) of claim 31 is construed to encompass both DNA and RNA, then for the reasons discussed above, the DNA aspect is probably a nullity and it is unclear whether the specification provides adequate guidance to enable those skilled in the art to make and use the mRNA that represents the remainder of the invention defined by part (b).

Finally, even assuming that part (b) of claim 31 were construed to encompass naturally occurring mRNAs that are at least 80% identical to SEQ ID NO:9, and assuming that the specification provides an enabling disclosure for such mRNAs, the scope of the claims would still be unclear. The specification provides no guidance that would allow those skilled in the art to determine, with a reasonable degree of confidence, whether any of the sequences that are at least 80% identical to SEQ ID NO:9 occur naturally and, if so, which they would be. The only way to definitely fix the scope of the claims would be to compare SEQ ID NO:9 to all naturally occurring sequences, clearly an impossible task. Thus, even if we were to ignore the various ambiguities discussed above, the metes and bounds of the claim are unclear.

As the Federal Circuit recently noted,

> [t]he Supreme Court explained the reason underlying the indefiniteness doctrine 60 years ago in United Carbon Co. v. Binney & Smith Co., 317 U.S. 228, 236, 55 USPQ 381, 385 (1942):

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[3] Sakharkar et al., "Distributions of exons and introns in the human genome," In Silico Biology, Vol. 4, page 0032 (June 16, 2004) (Epub ahead of print accessible at www.bioinfo.de/isb/2004040032/). Copy attached.

> A zone of uncertainty which enterprise and experimentation may enter only at the risk of infringement claims would discourage invention only a little less than unequivocal foreclosure of the field. Moreover, the claims must be reasonably clear-cut to enable courts to determine whether novelty and invention are genuine.

Exxon Research and Eng'g Co. v. United States, 265 F.3d 1371, 1376, 60 USPQ2d 1272, 1276 (Fed. Cir. 2001). The court held that compliance with 35 U.S.C. § 112, second paragraph, is determined by "whether 'the claims at issue [are] sufficiently precise to permit a potential competitor to determine whether or not he is infringing.'" Id. (bracketed text in original, quoting Morton Int'l, Inc. v. Cardinal Chem. Co., 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993)). That test is not met here.

For all these reasons, the scope of claim 31 is unclear. The test for definiteness is "whether one skilled in the art would understand the bounds of the claim when read in light of the specification." Miles Laboratories Inc. v. Shandon Inc., 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993). See also Amgen, Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1342, 65 USPQ2d 1385, 1406 (Fed. Cir. 2003): "[A]mbiguity in claim scope is at the heart of the definiteness requirement of 35 U.S.C. § 112, ¶ 2." Since we cannot determine the scope of claim 31, we conclude that it is indefinite. Claim 31 is rejected under 35 U.S.C. § 112, second paragraph.

Time Period for Response

This decision contains a new ground of rejection pursuant to 37 CFR § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 CFR § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 CFR § 41.50(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution.* Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . .
>
> (2) *Request rehearing.* Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

VACATED, 37 CFR § 41.50(b)

Sherman D. Winters)
Administrative Patent Judge)
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)
Donald E. Adams) BOARD OF PATENT
Administrative Patent Judge)
) APPEALS AND
)
Eric Grimes) INTERFERENCES
Administrative Patent Judge)

EG/jlb

Foley and Lardner
Suite 500
3000 K Street NW
Washington, DC 20007